REMARKS

Election/Restriction

Applicants acknowledge that the restriction requirement between Groups I and III has been dropped and that the species election has been extended to include Plasminogen activator inhibitor type I. Accordingly, Applicants have added new Claims 26 through 38 which are directed to the subject matter of Group III as identified in the previous Office Action mailed from the USPTO on April 4, 2006 (Claims 9-11, 14-16, 17-19 and 22-25 as originally filed).

Claim Objections

Claim 1 is objected to for the typographical error in which "associate" should be "associated". Claim 1 has been amended to overcome this objection. Claim 1 is also objected to as being drawn to non-elected subject matter. Claim 1 has been amended to overcome this objection.

Indefiniteness

Claims 1-3 and 6-8 are rejected as indefinite, because the claim as originally written, when cells are cultured under conditions that induce senescence does not include the presence and absence of the test compound. Claim 1 has been amended to recite "treating the mammalian cell in the presence and absence of the compound with an agent that induces senescence or culturing the mammalian cell in the presence and absence of the compound under conditions that induce senescence." Applicants respectfully submit that this amendment overcomes the rejection, and accordingly request that this rejection be withdrawn.

Anticipation

Claims 1, 2 and 7 are rejected as anticipated by Beug et al. (US 6,383,733). This rejection is further evidence by Yu et al., and Tremain et al. Applicants respectfully traverse this rejection.

To anticipate a claim, anticipation by a cited reference must be clear and unambiguous. It is not at all clear that the Beug reference anticipates the instant claims, because it is not at all clear that the culturing of the cells with TGFβ activates the PAI promoter through a CDK

inhibitor. It appears to be to the contrary. For example, Beug, at column 11, lines 34-50 reads as follows.

> This test cell, which is a human or animal cell, is stably transformed with a plasmid, in which a reporter gene, e.g. the luciferase gene, is under the control of the regulatory sequence of the PAI gene (or a gene which codes for another molecule regulated by TGFβ, e.g. for an extracellular matrix protein). The test cell is also transformed with the human type I or type II receptor, which was shown, after further tests, to be most efficient both at triggering the EF conversion and also at inducing PAI or another molecule regulated by TGFβ. The human TGFβ type II receptor used for the construction of the TβRII-dn is one of the possible target molecules for a TGFβ inhibitor. The control cell used is expediently a parallel clone in which the PAI-1 promoter controlled reporter gene is activated by another receptor not related to the TGFβ receptor.

Notably, for the Beug system to work, expression of the TGFβ receptor transgene is required. If another receptor is expressed in its place, it merely serves as a control. In the claimed invention, no construct encoding TGFβ is used or required. This strongly suggests that the system of Beug is acting quite differently than the claimed method.

This is further supported by the secondary references. Yu states that "We found that TNF-α but not TGF-β upregulates $p21^{waf1/cip1}$ expression". (emphasis added) Tremain adds, "Since $p21^{waf1}$ expression is elevated during senescence, and this does not appear to be mediated by TGFβ, it is likely that downstream signaling by p53 is intact." (emphasis added)

Taken together, culturing of the test cell with TGFβ, as taught by Beug, does not clearly and unambiguously utilize conditions that induce p21, and thus Beug does not anticipate the claimed invention.

Claims 1, 2, 6 and 8 are rejected as anticipated by Fisher and Jiang (US 6,051,376). In particular, col. 17, lines 45-50 of the reference are cited. Applicants note that Fisher does not include the claimed step of treating the cell with an agent that induces senescence or culturing the cell under conditions that induce senescence. To anticipate a claim, a single reference must set forth every limitation of the claim. Accordingly, Fisher cannot anticipate claims 1, 2, 6 and 8. Applicants respectfully request that this rejection be withdrawn.

Obviousness

Claim 3 is rejected as being obvious over Fisher and Jiang in view of Porter et al. As discussed above, Fisher is deficient in that it does not teach the step of treating the cell with an agent that induces senescence or culturing the cell under conditions that induce senescence. Porter et al. does not remedy this deficiency. Accordingly, Applicants request that this rejection be withdrawn.

Obviousness-type double patenting

Claims 1-3 and 6-8 are provisionally rejected for obviousness-type double patenting over claims 1, 2, 4-8 and 1-14 of US Patent No. 6,706,491. Applicants believe that this was not intended to be a provisional rejection, since the cited patent has been issued. Accordingly, Applicants will submit a terminal disclaimer to overcome this rejection once all other issues of patentability have been resolved.

Claims 1-3 and 6-8 are provisionally rejected for obviousness-type double patenting over claims 28-37 and 58-63 of co-pending application no. 10/233,032. This rejection is provisional because neither the presently pending claims nor the claims of the co-pending application have been allowed. Under PTO practice, this rejection will be withdrawn when all other issues of patentability have been favorably resolved. Accordingly, Applicants will not address this rejection at this time.

Claims 1-3 and 6-8 are provisionally rejected for obviousness-type double patenting over claims 25-30, 32, 33, 52-58, 95-101, 103-105 and 107-115 of co-pending application no. 09/861,925. This rejection is provisional because neither the presently pending claims nor the claims of the co-pending application have been allowed. Under PTO practice, this rejection will be withdrawn when all other issues of patentability have been favorably resolved. Accordingly, Applicants will not address this rejection at this time.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,

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